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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/941,997	08/29/2001	Qinwei Shi	1112-1-052CON	9957

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	11

DATE MAILED: 03/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/941,997	SHI ET AL.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *4-8 and 10-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Claims 4-8 and 10-15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 10. Claims 1-3 and 9 are under consideration in this office action.

Drawings

2. The drawings are objected to because of the reasons set forth in the attached PTOL-948. However, the corrections will not be held in abeyance and applicant must submit proposed drawing corrections in response to the requirement in the Office action.

Priority

3. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application(s) (whether patented or abandoned)

should also be included. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

Specification

4. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

5. The use of the trademark TENTAGEL ™ and other diagnostics and reagents have been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

6. The attempt to incorporate subject matter into this application by reference to 08/993,380 at page 3 and 08/862,613 and 08/961,858 at page 16 and the like as recited throughout the instant specification is improper because a mere reference to another application, is not an incorporation since the documents do not appear to be published. However, if the applications have been published, the patent number needs to entered in place of the serial number.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-3 and 9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claim 1 is drawn to an isolated polypeptide corresponding to an N-terminal fragment of human cardiac troponin I consisting of about 95 to about 115 amino acids. Claim 3 is drawn to the fragment comprised of SEQ ID NO:2.

The written description in this case only sets forth the specific sequence identified by SEQ ID NO:2 to which the claimed polypeptide should correspond, therefore the written description is not commensurate in scope with the claims drawn to fragments of troponin I. There is no teaching of what the isolated polypeptide is. The claims only recite what the isolated polypeptide must correspond to. There is no guidance as to what the fragments are, thus there is no guidance as to what the isolated polypeptide is. There is no guidance as to what amino acids must be comprised within the claimed fragment or which amino acids are required for a fragment to be considered as corresponding to an N-terminal fragment of cardiac troponin I, thus there is no guidance as to what the isolated polypeptide is. The specification does not include structural examples of the isolated polypeptide or the fragments to which the polypeptide corresponds. Thus, the resulting fragment could correspond to polypeptides

not taught and enabled by the specification. Furthermore, the claims fail to recite reference sequences upon which the fragment is based upon to teach the identity of the corresponding polypeptide.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

With the exception of the specifically identified SEQ ID NO:2, the skilled artisan cannot envision the detailed structure of the fragments, let alone the structure of the corresponding polypeptide. Thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. An adequate description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of molecules falling within the scope of the claimed genus.

The claims drawn to the polypeptide fragment fail to recite any associated function. Without an associated function there is no limit on the polypeptide encompassed by the claims. It is noted that there is no requirement that the polypeptide have inhibitory subunit activity, therefore any polypeptide that corresponds to the N-

terminal of troponin I meets the limitations of the claims. Furthermore any variant or mutant that has similar sequence identity yet has a different function is also encompassed by the claims. However, applicant has not taught examples of such polypeptides. In view of the structure of the fragments having not been adequately defined, the structure and function of the isolated polypeptide have not been defined by the instant specification.

Even though claim 3 recites a sequence identification number, the skilled artisan cannot envision the detailed structure of the encompassed polypeptide since the specification has not defined a reference sequence from where amino acids 95 to 115 are drawn. The specification has failed to define how the isolated polypeptide corresponds to the amino acids 95 to 115. Thus, a skilled artisan cannot envision the detailed structure of corresponding polypeptides.

Currently the claim drawn to an isolated polypeptide corresponding to an N-terminal fragment of human cardiac troponin I consisting of about 95 to about 115 amino acids, which lacks a function of the polypeptide is insufficient to support the claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645. Therefore, the full breadth of the claims fails to meet the written description provision of 35 USC 112, first paragraph.

8. Claims 2-4 and 8-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as

to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In particular, claim 1 is drawn to an isolated polypeptide corresponding to an N-terminal fragment of human cardiac troponin I consisting of about 95 to about 115 amino acids.

The specification fails to identify the isolated polypeptide that corresponds to the fragments of troponin I. There is no teaching of what the isolated polypeptide is. The claims only recite what the isolated polypeptide must correspond to. There is no guidance as to what the fragments are, thus there is no guidance as to what the isolated polypeptide is. There is no guidance as to what amino acids must be comprised within the claimed fragment or which amino acids are required for a fragment to be considered as corresponding to an N-terminal fragment of cardiac troponin I. Thus there is no guidance as to what the isolated polypeptide is. The specification does not include structural examples of the isolated polypeptide or the fragments to which the polypeptide corresponds. Thus, the resulting fragment could correspond to polypeptides not taught and enabled by the specification.

Several publications document the unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over biomolecules of related function upon a significant amount of further research. See the following publications that support this unpredictability as well as noting certain conserved sequences in limited specific cases: Russell [J. Mol.

Bio.244:332-350]; Skolnick et al., [Trends in Biotech, 18(1):34-39]; and Attwood, [Science, 290:471-473, (29 October 2000)].

In absence of further guidance from Applicants, the skilled artisan would have to de novo discover what the isolated polypeptide is and whether it corresponds to the troponin I fragments. Such experimentation requires ingenuity beyond that expected of one of ordinary skill in the art. The need for non-routine experimentation demonstrates that the specification is not enabled for any asserted use or well-established use for the isolated polypeptides. Therefore, a skilled artisan would be forced into undue experimentation to practice (i.e., make and use) the invention as is broadly claimed.

9. Claims 1-3 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are unclear and indefinite because the claims fail to recite the reference sequence upon which the recited amino acids are based upon. There is no recitation of a reference sequence for troponin I for which the amino acids 20 to 30 to about 95 to about 115 is based upon. Therefore, the claims are indefinite.

The term "corresponds" in the claims is a relative term which renders the claim indefinite. The term "corresponds" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The metes and bounds of the claim cannot be ascertained since it is unclear how the polypeptide is to

correspond to the fragment, i.e., by sequence identity, function or some other corresponding aspect. Therefore, the claims are rejected.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

10. Claims 1-2 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Morjana et al., (WO97/19955).

The claims are drawn to an isolated polypeptide corresponding to an N-terminal fragment of human cardiac troponin I consisting of about 95 to about 115 amino acids.

Morjana et al., (WO97/19955) teach that Troponin I exists in three isoforms, one being a cardiac Troponin I isoform with an additional 31 residues on the N-terminus (page 2 lines 9-14). Cardiac troponin I is found in human serum and can be used in immunoassays to test for human cardiac troponin I which is valuable to the medical community (page 2 lines 15-20). The invention teaches the use of a human cardiac troponin I fragment generated from human recombinant troponin I by chemical cleavage. The cleavage of the recombinant polypeptide uses cyanogen bromide, where this isoform results in a major polypeptide of 153 amino acids, represents 73% of the primary structure of human cardiac troponin I and is immunologically more reactive than

recombinant troponin I (page 3-4 lines 30-1). This isoform also has increased stability over the synthetic peptide used in other immunoassays (page 4 lines 9-10). Longer or shorter forms of this isoform can be produced by adding or deleting a few amino acids to/from the N-terminal, C-terminal or any part of the troponin I isoform (page 11 lines 30-33). Some changes in amino acids may not affect the isoforms performance (page 12 lines 5-6). The modified cDNA can give rise to the expression product for the isoform or its modified form (page 12 lines 2-4). Morjana et al., teach a sequence with 99.7% sequence homology to SEQ ID NO: 2 of the instant application.

Therefore, Morjana et al., teach an isolated polypeptide that corresponds to a human cardiac troponin I fragment comprised of about 95 to about 115 amino acids.

11. Claims 1-2 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Moses et al., (WO 97/30085).

The claims are drawn to an isolated polypeptide corresponding to an N-terminal fragment of human cardiac troponin I consisting of about 95 to about 115 amino acids.

Moses et al., teach human troponin subunit I and fragments thereof. The invention relates to therapeutic methods and compositions based on the troponin subunits (page 8 lines 15-17). The fragments can be at least 10 amino acids however the preferred embodiments are at least 50, 75, 100 or 120 amino acids long (page 10 lines 25-26). The peptides can be fast or slow twitch and cardiac isoforms form mammalian species such as human (page 11 lines 3-6). The troponin fragments can be made by altering the troponin sequences with substitutions, addition or deletions that provide for functionally equivalent molecules (page 12 lines 11-13). The fragment molecules can be at least 75, 120 or 200 amino acids (page 13 lines 1-5).

Therefore, Moses et al., teach isolated polypeptides corresponding to N-terminal fragments of human cardiac troponin I ranging from about 95 to about 115 amino acids.

12. Claims 1-3 and 9 are rejected under 35 U.S.C. 102(e) as being anticipated by Potter et al., (WO97/39132). Potter et al., (WO97/39132) teach stabilized preparations of human troponins. Troponins are proteins located on the actin thin filament of the vertebrate skeletal and cardiac muscles, where troponin I is the inhibitory subunit (page 1 lines 19-23). Cardiac and skeletal isoforms of troponin I are similar in their sequences, however the cardiac isoform differs substantially from its skeletal counterpart in possessing a 30-33 amino acid, species dependent N terminal extension (page 1 lines 26-28). Troponin proteins have previously been cloned, expressed and purified from *E. coli* expression vectors (page 2 lines 2-4). Example 1 teaches recombinant human cardiac troponin I that has 100% sequence homology to SEQ ID NO: 2 of the instant application.

Therefore, Potter et al., teach an isolated polypeptide that corresponds to a human cardiac troponin I fragment comprised of about 95 to about 115 amino acids.

Prior Art

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Hunkeler et al., teach the troponin I isoforms expression in the human heart. Vallins et al., teach molecular cloning human cardiac troponin I using polymerase chain reaction where the cardiac isoform has an extended N-terminal sequence.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is (703) 305-0487. The examiner can normally be reached on Monday through Thursday from 6:30am to 4:00pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Ja-Na Hines
March 11, 2003

LYNETTE R. F. SMITH
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